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EFFECT OF FREQUENT GENERIC IMATINIB SWITCHING ON TREATMENT RESPONSE IN PATIENTS WITH CHRONIC MYELOID LEUKEMIA

Murat Çınarsoy [1,*], Buğra Sağlam [2]

[1] *Şanlıurfa Mehmet Akif İnan Training and Research Hospital, Clinic of Hematology*
[2] *Medicalpoint Gaziantep Hospital, Clinic of Hematology, Stem Cell Transplant Unit*

Objective: The aim of this study was to evaluate the effect of switching one or more generic imatinibs during treatment on outcomes in patients with chronic phase chronic myeloid leukemia.. **Case Report:** Chronic myeloid leukemia (CML) is a myeloproliferative neoplasm associated with the Philadelphia chromosome t(9;22)(q34;q11) and the BCR::ABL1 fusion gene, which produces a constitutively active BCR::ABL1 tyrosine kinase.CML accounts for approximately 15 to %20 of adult leukemia. It has an annual incidence of 1 to 2 cases per 100,000, with a slight male predominance.The median age at presentation is approximately 50 years, and the prevalence of CML is steadily increasing in the Western world because of the dramatic effect of ABL1 kinase inhibitors on survival. Imatinib was the first commercially available TKI to approved by the U.S Food and Drug Administration (FDA) and the European Medicines Administration (EMA) for the initial treatment of CML. The high cost of new cancer drugs, including those developed for CML, is a major concern for healthcare payers, especially in countries with limited resources. Reimbursement policies around the world therefore encourage the use of generics to reduce prices.The European LeukemiaNet 2020 recommendation for the use of generic imatinib is as follows : "As long as a generic medicine meets the national standards of the country concerned in terms of quality of production, bioavailability and efficacy, it is an acceptable alternative to the branded product. *It is recommended that the patients continue to use the same generic brand whenever possible to avoid potential side effects due to changes in drug structure, bioavailability and excipients.*" In the NCCN guidelines, the recommendation for generic drugs is as follows: "Innovator and generic drugs approved by regulatory authorities on the basis of pharmacokinetic equivalence can be used interchangeably" and "*In countries where more than one generic drug is available, switching from one generic drug to another is not recommended*". **Methodology:** We retrospectively analyzed data from patients diagnosed with CML-CP treated with imatinib from 2010 - 2024. Patients with chronic phase chronic myeloid leukemia who were over 18 years of age and who started treatment with original or generic imatinib and switched to generic imatinib at any time during treatment were included. Patients who were diagnosed before the age of 18, patients whose treatment was interrupted during pregnancy, patients who did not use generic imatinib or patients who used only one brand of generic imatinib permanently were excluded from the study.The characteristics of the patients and the follow-up periods were collected retrospectively from the patients' electronic files.The efficacy of treatment was evaluated via standard hematological and molecular assessments to determine the rates of complete hematological response (CHR), molecular response (MR), and treatment failure, which was defined as a bcr-abl level of 1 % or higher on two occasions with an interval of one month. **Results:** A total of 46 patients, 26 (56.5%) male and 20 (43.5%) female (male/female ratio, 1.3), were included in the study. The median age was 45 years (range, 20-77 years). Forty-one (89.1%) of the patients were under 65 years of age, and 5 (10.9%) were over 65 years of age.The starting dose of imatinib was 400 mg/d in all patients. Treatment was started with Gleevec in 11 patients and generic imatinib in 35 patients. All patients were switched to two or more generic imatinibs during treatment.During the treatment process, 12 patients 2, 13 patients 3, 12 patients 4, 7 patients 5 and 1 patient 6 used different types of generic imatinib.Loss of response occurred in 8 of 46 (17.3%) patients. The earliest loss of response occurred at month 6, and the latest loss occured at year 9. One patient lost response at month 6, 1 patient at year 1, 2 patients at year 2, 1 patient at year 3, 2 patients at year 7, and 1 patient at year 9.All patients who experienced a loss of response responded to second-generation tyrosine kinase inhibitors, and none developed an accelerated or blastic phase. No dose increases or switches back to the original product in patients with loss of response. No patients had their dose changed or discontinued due to adverse events.When evaluated according to age, sex and number of generic imatinib switches, none of these variables were found to have any effect on response loss. **Conclusion:** Following the introduction of generic imatinib, several studies have shown that there is no loss of efficacy in patients who are switched from Glivec to generic imatinib. Although the ELN and NCCN CML guidelines do not discourage the use of generic imatinib, switching between generic imatinibs is not recommended. A review of both guidelines and the literature revealed no information on the development of adverse outcomes related to treatment response in patients switching between generic imatinibs.In the abovementioned retrospective studies, data on the responses obtained from patients receiving more than one type of generic imatinib were not shared.In our study, the response loss in patients who received more than one generic imatinib was 17.3%, which is comparable to the response losses observed in other studies of patients who received the original imatinib or generic imatinib.The findings of our study indicate that switching between generic imatinibs does not have a detrimental effect on treatment response.

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ONE CASE OF CHRONIC MYELOID LEUKEMIA IN PEDIATRIC GROUP

Nihal Boz [1,*]

[1] *Adana City Hospital*

Objective: Chronic myeloid leukemia (CML) is a myeloproliferative syndrome caused by monoclonal myeloid proliferation with the passage of immature granular elements into the peripheral blood. It is a rare disease in children and adolescents,

accounting for 2-3% of all leukemias in the pediatric population under the age of 15. (1) It is defined by the presence of a translocation (9;22), a cytogenetic abnormality associated with the disease. We report one of these rare cases because of its unusual frequency. **Case Report:** Fourteen year male child came to the pediatric hematology policlinic complaints of abdominal distension, bone pain and weakness. Clinical examination revealed mucocutaneous pallor and hepatosplenomegaly. The complete blood count received on the day of admission showed hyperleukocytosis at 178000/μL, normocytic normochromic anemia at 10,8 g/dl and thrombocytosis at 281000/μL. When the blood smear was examined, it was seen that there were myelocytes, metamyelocytes and promyelocytes, neutrophils and 4% myeloid-appearing blasts. Subsequent bone marrow aspiration showed hyperplasia of the neutrophilic granulocytic lineage at all stages of maturation, with promyelocyte, hyper granular myelocyte, metamyelocyte. (Figure 1) Cytogenetic analysis of the bone marrow as part of the etiological work-up confirmed the presence of the Philadelphia chromosome. Molecular testing for the BCR-ABL1 fusion transcript by RT-PCR on EDTA whole blood detected 64% (IS). The patient was admitted to the pediatric hematology service and started on hydroxyurea treatment. After the genetic diagnosis was confirmed, he was treated with Imatinib, a first-generation tyrosine kinase inhibitor (TKI). In the molecular evaluation performed at the 3-month follow-up, BCR-ABL1 fusion transcript was detected as 5% (IS) by RT-PCR. **Discussion:** Chronic myeloid leukemia (CML) is a rare hematological malignancy in the pediatric population. For treatment, our patient benefited from specific Imatinib therapy. According to the literature, Imatinib is the first-line drug.

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Adult Hematology Abstract Categories

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PAGET SCHROETTER SYNDROME AND HOMOZYGOUS FACTOR V LEIDEN MUTATION: A CASE PRESENTATION

Damla Cagla Patır [1,*], Nigar Abdullayeva [1], Dogus Berk Kuzucu [2], Mahmut Tobu [1]

[1] *Ege University Faculty of Medicine, Department of Hematology*
[2] *Ege University Faculty of Medicine, Department of Internal Medicine*

Case Report: Thrombosis in the deep veins of the upper extremity accounts for only 5% of symptomatic cases but constitutes approximately 50% of hospital-acquired thromboses. The vast majority of upper extremity thromboses, result from the presence of permanent venous catheter. Unprovoked cases are often secondary to "effort" thrombosis. Here, we present a case of Paget-Schroetter syndrome combined with a homozygous mutation of factor V Leiden. A 19-year-old female patient presented with pain and swelling in her right arm. The report of the right arm venous Doppler ultrasound indicated the presence of thrombus within the lumen at the proximal and distal segments of the basilic vein at the fossa cubiti level. The patient was found to have a homozygous mutation of factor V Leiden, and it was learned that she had been undergoing intense training and was engaged in water polo for the last two months. She had no history of medication use or chronic illnesses, nor any previous history of thrombosis. The patient was started on low molecular weight heparin for three months. A control Doppler ultrasound showed that the existing thrombus had resolved. It was recommended that the patient continue on her current anticoagulation with a new generation oral anticoagulant for one year. During this period, the patient, who ceased sports activities, did not develop any new thrombosis. The combination of young age, intense physical activity, especially in sports that utilize the upper extremities, and risk factors such as the factor V Leiden mutation strengthens the diagnosis. In the pathophysiology of this syndrome, vascular microtravma and exercise, muscle hypertrophy and thrombophilias contribute to the condition. Low molecular weight heparin and new generation oral anticoagulants are effective in preventing thrombosis formation and in inhibiting the growth of existing thrombus. Thrombolytic therapy may be considered in cases of large thromboses or severe symptoms.

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DESENSITIZATION TO RIVAROXABAN IN A PATIENT WHO EXPERIENCED ANAPHYLACTOID SHOCK AFTER ANTICOAGULANT USE: CASE REPORT

Damla Cagla Patır [1,*], Nigar Abdullayeva [1], Züleyha Galata [2], Umitcan Ates [2], Kutay Kırdok [2], Tugba Mermer [3], Sükriye Miray Bozgul [4], Reyhan Gumusburun [2], Elif Ertuna [5], Aytül Zerrin Sin [2], Mahmut Tobu [1]

[1] *Ege University Faculty of Medicine, Department of Hematology*
[2] *Ege University Faculty of Medicine, Department of Allergy and Immunology*
[3] *Ege University Faculty of Medicine, Department of Internal Medicine*
[4] *Ege University Faculty of Medicine, Department of Intensive Care*
[5] *Ege University Faculty of Pharmacy*

Case Report: Over the last two decades, new anticoagulants have been developed to prevent and manage thromboembolic diseases, including direct-acting anticoagulants like rivaroxaban, which is used for venous thromboembolism prevention, stroke prevention in atrial fibrillation, and ischemic heart disease. Here, we present the experience of a case with a history of multiple thromboses and an anaphylactoid reaction to anticoagulants, who was able to continue prophylaxis without allergic reactions after rivaroxaban desensitization. A 42-year-old female patient visited the hematology outpatient clinic to obtain a prescription for a new anticoagulant due to a supply issue with her current medication, fondaparinux..